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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,435	03/20/2001	Kerstin Krieglstein	MBP-005XX	1324

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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/786,435	KRIEGLSTEIN, KERSTIN	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 14-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *5/1/07*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Upon further review, consideration and the telephonic interview held May 1, 2007, the Advisory action mailed April 2, 2007 had been VACATED. The finality of the Final office action mailed December 19, 2006 has been withdrawn. A non-final action is set forth below:

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 16-18 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 16 depends from claim 1. Claims recites "said second compound...". There is insufficient antecedent basis for limitation because claim 1 does not recite "first compound". Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 14-15 are rejected under 35 U.S.C. 102(b) as anticipated by Logan et al *(WO 93/19783, published October 14, 1993).*

Claims 1 and 14-15 are drawn to a method for treating damaged neurons in a patient said damaged neurons caused by a cerebral disorder said method comprising the steps of: providing a patient having damaged neurons, said damaged neurons caused by a cerebral disorder; and administering to said patient a therapeutically effective amount of a compound that inhibits the biological activity of transforming growth factor-β1 (TGF-β1), transforming growth factor-β2 (TGF-β2) and/or transforming growth factor-β3 (TGF-β3) on damaged neurons in a cerebral disorder, thereby treating said damaged neurons in said patient by preventing neuronal apoptosis.

Logan et al teach that the present invention generally relates to CNS injuries and more particularly the presence of TGF-β1 in injured CNS tissues (page 3). Logan et al teach that the there is a potential use for TGF-β1 antagonists (inhibitors) as adjunct to those therapies designed to promote regeneration and reconnection of damaged neural pathways (page 8). Logan et al teach that antagonists include neutralizing TGF-β1 antibodies, decorin and its functional equivalents such as biglycan (page 3). Therefore the prior art reference teaches preventing apoptosis. Logan et al teach that animals underwent a craniotomy (example II). Logan et al teach that three days after the induced injury, oedma in the wound was still extensive (Example VI). Logan et al teach that neutralizing antibodies were infused into the wound (Example III, page 19). Logan et al teach that after infusion of the wound with neutralizing antibodies(anti-TGF-β1 antiserum), there was complete absence of immunoreactive fibronectin within the

wound and a reduced number of macrophage/microglial cells when compared to control (page 20). Therefore, Logan et al teach a method of treating damaged neurons (pages 20-21). Logan et al anticipate the claimed invention.

4. Claims 1, 14-15 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by Melton et al *(WO 95/10611, published April 20, 1995).*

Claims 1, 14-15 and 18 are drawn to a method for treating damaged neurons in a patient said damaged neurons caused by a cerebral disorder said method comprising the steps of: providing a patient having damaged neurons, said damaged neurons caused by a cerebral disorder; and administering to said patient a therapeutically effective amount of a compound that inhibits the biological activity of transforming growth factor-β1 (TGF-β1), transforming growth factor-β2 (TGF-β2) and/or transforming growth factor-β3 (TGF-β3) on damaged neurons in a cerebral disorder, thereby treating said damaged neurons in said patient by preventing neuronal apoptosis.

Melton et al teach the a method of preventing or antagonizing a signal pathway in a cell for a growth factor of transforming growth factor β (TGF-β)(page 4). Melton et al teach that the antagonizing agent can inhibit the biological activity of the TGF-β type growth factor, for example, preventing the growth factor from binding its receptors on the surface of the treated cells (page 4). Melton et al teach that the antagonizing agent is selected from the group consisting of follistain module, and a truncated receptor for growth factor TGF-β family (page 4). Melton et al teach that the antagonizing agent of the invention can bind to growth factor and sequesters the growth factor such that it

cannot bind its receptors (page 4). Melton et al teach that the invention can be used to treat neurodegenerative disorders including anoxia-ischemia (page 5). Melton et alt each that the method comprising contacting a cell wither in vivo or in vitro with an agent cable of antagonizing the biological action of a protein from the family of transforming growth factor -β (page 5). Melton et al teach that the antagonizing agents can be administered by many administration routes such as intravenous and oral administration (page 19). Melton et al teach that the present method is amenable to therapeutic application of neurodegenerative disorders that are progressive and persistent loss of neuronal cells such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerois and Huntington's disease (page 6). Melton et al anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 1 and 14-17 are rejected under 35 U.S.C. 103(a) as unpatentable over Logan et al *(WO 93/19783, published October 14, 1993)* in view of Alexander et al *(Neurosurgery, 1990, 26/4, p. 559-564).*

Claims 1 and 14-17 are drawn to a method for treating damaged neurons in a patient said damaged neurons caused by a cerebral disorder said method comprising

the steps of: providing a patient having damaged neurons, said damaged neurons caused by a cerebral disorder; and administering to said patient a therapeutically effective amount of a compound that inhibits the biological activity of transforming growth factor-β1 (TGF-β1), transforming growth factor-β2 (TGF-β2) and/or transforming growth factor-β3 (TGF-β3) on damaged neurons in a cerebral disorder, thereby treating said damaged neurons in said patient by preventing neuronal apoptosis, wherein the method of 16, wherein said second compound is selected from the group consisting of urokinase, thrombin and tissue plasminogen activator.

Logan et al that the present invention generally relates to CNS injuries and more particularly the presence of TGF-β1 in injured CNS tissues (page 3). Logan et al teach that the there is a potential use for TGF-β1 antagonists (inhibitors) as adjunct to those therapies designed to promote regeneration and reconnection of damaged neural pathways (page 8). Logan et al teach that animals underwent a craniotomy (example II). Logan et al teach that three days after the induced injury, oedma in the wound was still extensive (Example VI). Logan et al teach that neutralizing antibodies were infused into the wound (Example III, page 19). Logan et al teach that after infusion of the wound with neutralizing antibodies(anti-TGF-β1 antiserum), there was complete absence of immunoreactive fibronectin within the wound and a reduced number of macrophage/microglial cells when compared to control (page 20). Therefore, Logan et al teach a method of treating damaged neurons (pages 20-21).

Logan et al do not teach the claim limitations the method of 16, wherein said second compound is selected from the group consisting of urokinase, thrombin and tissue plasminogen activator.

Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage (see the Abstract). Alexandria et al teach that tissue plasminogen activator is effective in lysing blood clots in animals (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the urokinse or tissue plasminogen activator of Alexandria et al to the pharmaceutical compositions used in the method of Logan et al because Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage such as the patients with CNS pathologies as taught by Logan et al and Alexander et al has shown that tissue plasminogen activator is effective in lysing blood clots in animals. It would be expected absent evidence to the contrary, that the addition of urokinase or tissue plasminogen activator would disintegrate blood clots because it is well known in the art that the prevention of blood clots would be necessary for treatment of central nervous systems disorders.

6. Claim 1, 14-16 and 17-18 are rejected under 35 U.S.C. 103(a) as unpatentable over Melton et al *(WO 95/10611, published April 20, 1995).* in view of Alexander et al *(Neurosurgery, 1990, 26/4, p. 559-564).*

Claims 1, 14-15 and 17-18 are drawn to a method for treating damaged neurons in a patient said damaged neurons caused by a cerebral disorder said method comprising the steps of: providing a patient having damaged neurons, said damaged neurons caused by a cerebral disorder; and administering to said patient a therapeutically effective amount of a compound that inhibits the biological activity of transforming growth factor-β1 (TGF-β1), transforming growth factor-β2 (TGF-β2) and/or transforming growth factor-β3 (TGF-β3) on damaged neurons in a cerebral disorder, thereby treating said damaged neurons in said patient by preventing neuronal apoptosis, wherein the method of 16, wherein said second compound is selected from the group consisting of urokinase, thrombin and tissue plasminogen activator.

Melton et al teach a method of preventing or antagonizing a signal pathway in a cell for a growth factor of transforming growth factor β (TGF-β)(page 4). Melton et al teach that the antagonizing agent can inhibit the biological activity of the TGF-β type growth factor, fro example preventing the growth factor from binding its receptors on the surface of the treated cells (page 4). Melton et al teach that the antagonizing agent is selected from the group consisting of follistain module, and a truncated receptor for growth factor TGF-β family (page 4). Melton et al teach that the antagonizing agent of the invention can bind to growth factor and sequesters the growth factor such that it cannot bind its receptors (page 4). Melton et al teach that the invention can be used to treat neurodegenerative disorders including anoxia-ischemia (page 5). Melton et alt each that the method comprising contacting a cell wither in vivo or in vitro with an agent cable of antagonizing the biological action of a protein from the family of transforming

growth factor -β (page 5). Melton et al teach that the antagonizing agents can be administered by many administration routes such as intravenous and oral administration (page 19). Melton et al teach that the present method is amenable to therapeutic application of neurodegenerative disorders that are progressive and persistent loss of neuronal cells such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerois and Huntington's disease (page 6).

Melton et al do not teach the claim limitations the method of 16, wherein said second compound is selected from the group consisting of urokinase, thrombin and tissue plasminogen activator.

Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage (see the Abstract). Alexandria et al teach that tissue plasminogen activator is effective in lysing blood clots in animals (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the urokinse or tissue plasminogen activator of Alexandria et al to the pharmaceutical compositions used in the method of Melton et al because Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage such patient that would have the disorders as disclosed by Melton et al and Alexander et al has shown that tissue plasminogen activator is effective in lysing blood clots in animals. It would be expected absent evidence to the contrary, that the addition of urokinase or tissue plasminogen activator would disintegrate blood clots because it is well known in the art

that the prevention of blood clots would be necessary for treatment of central nervous systems disorders.

Status of Claims

7. No claims are allowed.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vanessa L. Ford
Biotechnology Patent Examiner
August 17, 2007

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PRIMARY EXAMINER